Myocardial perfusion occurs primarily in diastole since systolic contraction transiently impedes coronary blood flow especially to the subendocardium. Thus, myocardial bridges replicate the normal microvascular physiology of high diastolic and low systolic flow, albeit at the level of the epicardial coronary artery. Because marked myocardial bridges are not common during invasive angiography, and hence “abnormal,” they have the potential to trigger a similar “oculusstenotic” reflex typical for atherosclerotic stenosis.

As a relative coronary flow reserve (rel CFR) derived from pressure measurements, fractional flow reserve (FFR) to guide percutaneous coronary intervention has redefined coronary stenosis “severity” from anatomy to physiology, although the journey took 20 years. Similarly, the severity and effects of myocardial bridges are even more appropriately defined by physiology than anatomy. The physiologic dynamics of myocardial bridges reflect time-varying interactions among aortic pressure, arterial and myocardial compression, diastolic flow, transmural perfusion gradients, heart rate or diastolic perfusion time, and sympathetically driven myocardial contraction and coronary vasoconstriction, all interacting with diffuse and focal atherosclerotic disease that is beyond anatomic description.

THE CURRENT REPORT

Therefore, Uusitalo et al. (8), in this issue of *iJACC*, deserve congratulations for this first systematic study of quantitative perfusion and CFR by positron-emission tomography (PET) in adults with myocardial bridging. The protocol included 100 patients with potential coronary artery disease (CAD) undergoing computed tomographic angiography, PET myocardial perfusion imaging at rest and during vasodilator stress, and invasive coronary angiography; 34 of these patients had 48 coronary artery myocardial bridges classified as superficial in 24 (>1- to 2-mm deep) or deep in 24 (>2-mm deep). CAD was assessed by computed tomography soft or calcified plaque, or by quantitative coronary angiography of atherosclerotic percent diameter stenosis. Myocardial bridging was identified by systolic compression of the coronary artery using visual assessment and quantified by quantified coronary angiography of diastolic and systolic angiographic frames.
INSTRUCTIVE FLAWS

The strength of the study derives from being technically well done by an experienced group with a clear conclusion for the selected population of all patients with angiographic myocardial bridges identified by screening computed tomographic angiography. The results are clinically important for showing that most myocardial bridges cause no impairment of coronary blood flow, no ischemia, and no accelerated atherosclerosis, and require no procedures. In essence, the study shows that myocardial bridges are not uncommon, but they are without anatomic or physiologic significance, and are benign and therefore best ignored.

However, as the authors acknowledge, some bridges reportedly associate with angina and stress perfusion abnormalities relieved by percutaneous coronary intervention or surgical excision. By importantly showing that nearly all bridges are physiologically and anatomically benign with normal exercise stress, the study does not include enough severe symptomatic bridging to define their pathophysiology.

Prior references in their paper document myocardial ischemia in patients with “severe” 50% or 75% diameter systolic narrowing caused by myocardial bridging. By contrast in the current study, the authors report predominantly 50% diameter bridge stenosis that, given the variability of measurement, likely reflects mild stenosis due to myocardial bridging having no impact on coronary blood flow. FFR at the bridge was not measured.

Dobutamine and exercise stress have markedly different effects than adenosine or vasodilator stress on coronary artery stenosis (9,10) and particularly myocardial bridges (11–13). The sympathetic drive of dobutamine or exercise causes tachycardia that shortens diastolic perfusion time, increases epicardial coronary vasoconstriction and contraction of myocardial bridges along with the rest of the myocardium as mechanisms whereby myocardial bridges may compress the epicardial artery, inhibit flow, and cause ischemia. This study by Uusitalo et al. (8) using adenosine vasodilator stress PET perfusion imaging importantly showed the benignity of most myocardial bridges. However, their choice of vasodilator stress precludes examining the pathophysiology of ischemia caused by myocardial bridges as reviewed below.

WHAT ELSE DO WE NEED TO KNOW?

Complete physiological understanding requires data driven explanation for both the benign myocardial bridging as in this paper but also for the uncommon myocardial bridge causing ischemia. If the

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**FIGURE 1** Schematic of Coronary Artery Flow and Transmural Distribution

(A) Schematic of coronary artery flow. Coronary artery flow at rest (dashed pink line) and during stress hyperemia and tachycardia (solid pink line). The stress hyperemic response may be severely blunted (blue line) by severe myocardial bridge compression of the epicardial artery and dynamic severe stenosis that limits coronary flow reserve (CFR) with low distal fractional flow reserve (FFR). For mild to moderate myocardial bridge compression causing mild to moderate stenosis, the stress hyperemic response may be only moderately blunted (green line).

(B) Differential perfusion to subepicardium versus subendocardium. Differential perfusion to the subendocardium compared to the subepicardium is due to time delay in subendocardial hyperemia, here shown in a normal non-stenosis experimental model (adapted with permission from Downey et al. [5]). At the time of initial high subepicardial hyperemia reaching 100% of its peak, the subendocardial hyperemia has reached only 45% of its peak. Arterial compression or stenosis that impedes the rapid early diastolic hyperemia and tachycardia that shortens diastolic perfusion time exacerbates this normal delay in subendocardial hyperemia.
pathophysiology driving the clinical problem is not addressed or accounted for in a randomized trial of interventions on generic anatomic myocardial bridging, the outcomes would likely show little benefit or even harm from potential stent fracture or risk of surgery.

Other than their being usually benign, what do we not know about myocardial bridging that is important to clinical pathophysiology but remains poorly defined for management decisions? Simple systolic compression of coronary arteries that reduces systolic flow is not physiologically logical for the following reasons. Normally, systolic myocardial compression of the microcirculation stops transmural myocardial perfusion in systole (except perhaps in a small layer of epicardium) followed by early diastolic hyperemic perfusion. If myocardial bridges behave like normal myocardium that relaxes in diastole enough to allow high hyperemic diastolic flow, then myocardial bridges should cause no impairment of the predominantly diastolic flow necessary to prevent ischemia.

**PATHOPHYSIOLOGY OF MYOCARDIAL BRIDGES**

Consequently, the rare myocardial bridge causing ischemia must incur additional complex pathophysiology via compression of the epicardial coronary artery beyond systole into diastole enough to impair flow to the myocardium or due to some other mechanism. The sympathetic drive during dobutamine or exercise may prolong the myocardial bridge contraction (delayed relaxation) beyond systole that impairs early hyperemic diastolic flow in addition to tachycardia shortening diastolic perfusion time, shown in Figure 1A, thereby causing ischemia. Figure 1B shows the profound delay in subendocardial perfusion (5).

**FIGURE 2** Pullback Fractional Flow Reserve and Flow Velocity Across Myocardial Bridges

(A) Fractional flow reserve and (B) flow velocity were measured distal to, within, and proximal to myocardial bridges during dobutamine stress. Reproduced with permission from Lin et al. (11). dFFR = diastolic fractional flow reserve.
making it more subject to ischemia than the sub-epicardium as seen in severe left ventricular hypertrophy or moderate to severe structural coronary artery stenosis. Alternatively, myocardial bridge contraction might cause localized phasic coronary artery spasm that persists into diastole since the time constants for changes in arterial vascular smooth muscle are slower than the duration of diastole, especially with tachycardia of exercise.

This dual impairment of diastolic flow—inhibition of early rapid diastolic hyperemia and shortened diastolic perfusion time—has 2 secondary pathophysiological consequences depending on the heart rate, severity, and duration of the epicardial arterial compression.

The most uncommon extreme of these consequences is transmural or subendocardial ischemia downstream of severe arterial bridge compression like any severe, dynamic coronary artery stenosis thereby causing a low FFR with dobutamine stress but normal FFR with adenosine stress (11-13). For such severe low FFR, dobutamine stress would likely cause a corresponding PET perfusion while vasodilator stress may not, paralleling the low FFR with dobutamine but not adenosine (11-13). Myocardial perfusion images with exercise are worse than with adenosine stress due to sympathetic vasoconstriction in addition to structural stenosis (9,10).

The more likely, less extreme of these unusual circumstances is septal ischemia documented in remarkable detail due to depressurization of septal branches within the myocardial bridge associated with high velocity in the compressed arterial segment. This intra-bridge high flow velocity is associated with decreased intra–bridge perfusion pressure to the septal branch, called the “Venturi” effect by the authors, shown in Figure 2 (11). It is a special example of a more general fluid dynamic phenomenon called “branch steal” described for the epicardial coronary artery branches experimentally and clinically by PET perfusion imaging (14). This pathophysiology of myocardial bridges is associated with a “buckling” pattern of septal motion on dobutamine echocardiography (11).

Figure 3 shows the simple, severe arterial bridge compression like any severe dynamic stenosis causing ischemia in the downstream arterial distribution. Here, it is modeled as a 67% diameter stenosis due to myocardial bridge compression causing low FFR and a potential regional perfusion abnormality (15,16). The stenosis shown as a fixed 67% diameter narrowing (in black) may be more severe during isometric left ventricular contraction and less severe during mid to late diastole due to phasic bridge compression (red overlay). Another alternative is only mild to moderate bridge compression with dynamic diameter stenosis averaging 55% diameter narrowing in this schematic that may cause septal “branch steal” (14) with isolated septal ischemia but adequate CFR and FFR downstream of the epicardial artery.

Septal branch steal may be due to dynamically changing bridge compression of the epicardial artery, to fixed structural stenosis, or to dynamic coronary vasoconstriction. The essential common pathophysiology is decreased perfusion pressure at the origin of the septal branch due to high intrastenosis flow velocity that reduces perfusion pressure to the septal branch due partially to a “Venturi effect” (11) but mostly due to classical fluid dynamic entrance and viscous pressure loss in the narrowed section causing “branch steal” (14).

The term branch steal (14) derives from the decrease in perfusion pressure to the septal branch and corresponding decrease in perfusion below resting levels such that the epicardial flow increases while septal flow decreases thereby “stealing” flow from the septal branch. Delayed diastolic septal relaxation would further inhibit septal flow during
low septal perfusion pressure. This dynamic bridge pathophysiology is identified by an FFR pullback across the myocardial bridge as in Figure 2 (11), or by an isolated septal defect on PET perfusion imaging with dobutamine stress.

However, for Figure 2 (11), the claimed contribution of Venturi pressure loss associated with observed intrastenosis flow velocities of 150 to 200 cm/s in the narrowed section (Figure 2) is only approximately 5 mm Hg. Therefore, the major intrastenosis measured pressure loss in Figures 2 and 3 is due to classical fluid dynamic entrance and viscous loss. The additional Venturi pressure loss at these relatively low flow velocities plays only a small role, contravening those authors (11) invoking the Venturi effect as the mechanisms for the decreased intrastenosis pressure. The branch steal mechanism still applies due to the lowered intrastenosis pressure regardless of the mechanism causing that lowered intrastenosis pressure.

**PHYSIOLOGICAL TEST FOR MYOCARDIAL BRIDGES TO GUIDE MANAGEMENT?**

This analysis and current literature suggest the following conclusions: 1) myocardial bridges are common, benign and rarely necessitate testing or intervention; 2) for questions of clinical significance, physiologic assessment trumps angiographic anatomy; and 3) when clinically indicated, the following physiologic tests may provide definitive answers to severity of myocardial bridges causing ischemia, all subject to further confirmation and trial: 1) dobutamine PET perfusion imaging for regional abnormalities in arterial distribution or isolated septal defects paralleling dobutamine stress induced abnormal FFR pull back tracings across the myocardial bridge not seen with vasodilator stress; 2) dobutamine FFR distal to the myocardial bridge recording intracoronary pressure during pull back within the myocardial bridge into the proximal artery to the aorta for measures of distal coronary pressure, intrastenosis pressure, and proximal pressure (for proximal diffuse disease); the pattern of pressure pullback pattern shown in Figure 2 suggests a hemodynamically significant myocardial bridge; and 3) the septal buckling pattern reported in association with the FFR pullback measurements of Figure 2 may be another noninvasive approach needing more complex PET or invasive evaluation (11).

In conclusion, the evidence is quite clear that for assessing myocardial bridges, physiology trumps anatomy, just as for structural coronary artery stenosis.

**REFERENCES**


**KEY WORDS** coronary atherosclerosis, fractional flow reserve, myocardial bridges, myocardial perfusion, PET